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Use of Statin and Target Low-density lipoprotein cholesterol attainment among post-ST elevation myocardial infarction patients in Shahid Gangalal National Heart Centre, Kathmandu, Nepal

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ABSTRACT

Background: and objective: Lipid-lowering is an important intervention to reduce cardiovascular morbidity and mortality in the secondary prevention of STEMI. There is no study to analyze the use of statin and LDL-C treatment target attainment among STEMI patients in Nepal. This study aims to assess the use of statin and LDL-C treatment target attainment among STEMI patients.

Methods: It was a prospective observational single-center study conducted at the Shahid Gangalal National Heart Centre, Kathmandu, Nepal outpatient department. An outpatient department-based survey was conducted among STEMI patients who have lipid profile levels at the time of admission for STEMI and after 4-13 weeks of the index event. Lipid profile levels, diagnosis, and risk factors were collected during the outpatient follow-up.

Results: Our study included 280 post-STEMI patients; the mean age was 57.5±11.7 years with the majority being male. The mean duration of follow-up was 6.7 ± 0.1 weeks. Rosuvastatin was the preferred statin with 82.1%. The most common dose of statin used was Rosuvastatin 20mg (70%), followed by Atorvastatin 40mg (12.5%). LDL-C levels of <1.4mmol/l were achieved in 44.6% of cases and LDL levels of <1.8mmol/l in 71.8% of cases. In 36.8% of the study population, there was a greater than 50% decline in LDL-C levels. Diabetic patients (55.1% and 83.1%) only have the significant achievement of LDL goal of both <1.4mmol/l and <1.8mmol/l respectively, when compared to those without diabetes (44.9% and 16.9%).

Conclusions: Most of the post-STEMI patients were treated with high doses of statins and achieved the target LDL-C levels.

Keywords: Atorvastatin; Low-density lipoprotein cholesterol; Rosuvastatin; STEMI.

INTRODUCTION

The 2018 American College of Cardiology (ACC) guideline on the management of blood cholesterol suggests that patients with recent acute coronary syndrome need to be treated with a high-intensity statin to lower LDL-C levels by [3]50% and aim for the LDL-C level<1.8mmol/L.[1] It also suggests that assessing adherence and response to LDL-C–lowering medications and lifestyle changes with repeat lipid measurement 4 to 12 weeks after statin initiation. European guidelines in 2019 lowered the recommended target LDL-C from<1.8mmol/L to <1.4mmol/Lfor secondary prevention of CAD.[2] Despite well-intended recommendations and strong evidence, the LDL-C target of <1.8mmol/L (70mg/dL) had only been achieved in 21% of the patients in registries.[3,4]

To date, there is no study analyzing the use of statin and LDL-C treatment target attainment among ST-elevation myocardial infarction (STEMI) patients in Nepal. This study aims to assess the use of statin and LDL-C treatment target attainment among STEMI patients.

METHODS

It was a prospective observational single-center study conducted at the SGNHC–outpatient department from January 2021 to March 2022. An outpatient department-based survey was conducted among STEMI patients who have lipid profile levels at the time of admission for

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STEMI and after 4-12 weeks of the index event. Lipid profile levels, diagnosis, and risk factors were collected during the outpatient follow-up.

With the precision (d) of 5% and 95% confidence interval and using the prevalence (P) of 21 % from the international study [3], using the formula N=Z2P(1-P)/d2, where Z is the Z statistic for the level of confidence 95%, the sample size was calculated to be 255. With an anticipated 10% dropout rate, our sample size was 280.

STEMI Patients who are under follow-up. Age of more than 18 years.

Refusal of participation in the study. Diagnosed as non-ST elevation MI and Unstable Angina patients.

The study was conducted after the ethical approval from the Institutional Review Board of SGNHC and informed consent from the patient. All patients who were under follow-up after the treatment of STEMI and fulfilled the inclusion criteria were enrolled. Baseline clinical characteristics such as age, sex, risk factors such as smoking, hypertension, diabetes mellitus, and family history of premature CVD were recorded.

Defined as chronic use of antihypertensive drugs or a previously documented blood pressure of 140/90 mmHg for non-diabetics and 130/80 for diabetics from medical records measured on at least two occasions.[5]

Patients previously diagnosed with Diabetes Mellitus (DM) or on oral hypoglycemic drugs or Insulin or newly diagnosed DM fulfilling the diagnostic criteria for DM as below, with or without other cardiovascular risk factors (e.g., smoking, hyperlipidemia, etc.).

Patients with symptoms suggestive of DM (Polyuria, polydipsia, weight loss) with at least one of the following:

Fasting plasma glucose ≥7.0 mmol/L (126mg/dl)

Random plasma glucose (or 2 hrs. after an ideal OGTT) ≥11.1 mmol/L (200mg /dl)

(In asymptomatic patients, at least two samples are required to confirm the diagnosis).[6]

Family History of premature Cardio Vascular Disease (CVD): history of CVD at age <55 years in first-degree male relatives and <65 years in first-degree female relatives.

Smoking status: As per the national health interview survey by the Centre for disease control and Prevention, [7] smokers were classified as:

Current smokers: One who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes

Ex-smoker: one who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of the interview.

Non-Smoker: One who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime.

Tobacco Chewer those whose chew tobacco

The Intensity of Statin Therapy: High-intensity statin and moderate-intensity statin is defined as per ACC 2018 and ESC 2019 Guidelines.

RESULTS

Among the 280 total study population, the mean age was 57.5±11.7 years with the majority being male 220 (78.6%). The mean duration of follow-up after the treatment was 6.7 ± 0.1 weeks. Among the risk factors; Hypertension was present in 127 (45.4%), Type 2 Diabetes Mellitus was present in 89 (31.8%), and Family history of CAD in 13(4.6%). Current smoker in 110 (39.3%), Ex-smoker 26 (9.3%), and Tobacco Chewer in 7 (2.5%) cases. Inferior wall myocardial infarction was the most common 133 (47.6%), followed by anterior wall MI 91(32.5%). Most of the patients (90.7%) underwent coronary angiography. Among the patient who underwent CAG most common finding was SVD in 113 (40.3%), DVD 85 (30.3%), TVD 53 (19%) Non-critical 2 (0.7%) TVD with Left main in 1 (0.4%) cases. Patients were medically managed in 16.3% of the cases and the remaining 83.7% underwent invasive therapy. Primary PCI was performed in 58.6% of the study population. Rosuvastatin was the preferred statin with 230 (82.1%) prescriptions among total STEMI patients. The remaining 50 (17.9%) received Atorvastatin. The most common dose of statin used was Rosuvastatin 20mg 190 (70%), followed by Atorvastatin 40mg 35 (12.5%), and Rosuvastatin 40mg 30 (10.7%). Atorvastatin 80mg 2 (0.7%) was the least used statin dose in the study population. Rosuvastatin 10 mg was used in 4 (1.5%) cases.Atorvastatin 20 mg was used in 13 (4.6%) cases.

Table 1 depicts the change in lipid parameters after treatment with statin during follow-up. Only the total cholesterol level and LDL-C level had a significant decrease with a p-value <0.001.

Table 1. Change in lipid parameters after treatment with the statin.

	Before Treatment N=280			After Treatment N=280			Change in Parameters*	
	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	p-value
Total Cholesterol (TC) in mmol/L	4.4 ± 1.1	2.1	9.0	3.3 ± 0.7	1.5	6.3	1.1 ± 1.1	<0.001
Triglycerides (TG) in mmol/L	1.7 ± 0.8	0.7	5.9	1.7 ± 0 .8	0.4	6.6	0.004 ± 0.80	0.927
High-density Lipoprotein) (HDL) in mmol/L	1.0 ± 0.2	0.6	1.5	0.9 ± 0.2	0.5	1.7	0.005 ± 0.22	0.672
Low-density Lipoprotein) (LDL) in mmol/L	2.582 ± 0.9439	0.8	7.5	1.5 ± 0.6	0.3	4.9	1.06 ± 0.94	<0.001

*Paired t-test

Among the study population, 125 (44.6%) achieved an LDL-C level below 1.4mmol/l. Table 2 shows the difference in the proportions of patients achieving LDL below 1.4mmol as compared to those who did not (>1.4mmol) after the treatment with statins. The difference was assessed for relevant CVD risk factors and management-related conditions Comparing the change in the different conditions, only patients with DM had a significantly higher proportion of patients (55.1% vs 44.9%) achieving the LDL goal of less than 1.4mmol/l (P= 0.024). For other characteristics such as HTN, history of smoking, family history of CAD, and different doses of statins, no significant difference was observed between those who achieved an LDL goal of less than 1.4mmol/l and those who didn't.

Table 2.Difference in the proportions achieving required LDL levels of <1.4mmol/L and those who didn't for different clinical and management related characteristics.

Values of LDL in mmol/L		<1.4	≥1.4	p-value
Conditions		n (%)	n (%)	
HTN	Yes	62 (48.8)	65 (51.2)	0.246
	No	63 (41.2)	90 (58.8)	
DM	Yes	49 (55.1)	40 (44.9)	0.024
	No	76 (39.8)	115 (60.2)	
Smoking	Current Smoker/Tobacco User	46(39.3)	71(60.7)	0.162
	Non-Smoker/Ex-Smoker	79 (48.5)	84(51.5)	
Family History of CAD	Yes	4 (30.8)	9 (69.2)	0.396
	No	121 (45.5)	145 (54.5)	
Type of Statin used	Rosuvastatin	106 (46.1)	124 (53.9)	0.376
	Atorvastatin	19 (38.0)	31 (62.0)	
Atorvastatin dose used	Atorvastatin 20mg	7 (53.8)	6 (46.2)	0.245
	Atorvastatin 40mg	12 (34.3)	23 (65.7)	
	Atorvastatin 80mg	0 (0.0%)	2 (100)	
Rosuvastatin dose used	Rosuvastatin 10mg	3 (75)	1 (25)	0.214
	Rosuvastatin 20mg	86 (43.9)	110 (56.1)	
	Rosuvastatin 40 mg	17 (56.7)	13 (43.3)	

Two hundred one study subjects (71.8%) achieved an LDL-C target of less than 1.8mmol/l in our study. Table 3

demonstrates the difference in the proportions of patients achieving LDL below 1.8 mmol as compared to those who did not (> 1.8 mmol) after the treatment with statins. The difference was assessed for relevant clinical and management-related conditions. Among the different conditions, only patients with DM had a significantly higher proportion of patients (83.1% vs 16.9%) achieving the LDL goal of less than 1.8mmol/l (P= 0.006).

Table 3. Difference in the proportions achieving required LDL levels of <1.8mmol/L and those who didn't for different clinical and management-related characteristics.

Values of LDL in mmol/L		<1.8	≥1.8	p-value
		n (%)	n (%)	
HTN	Yes	94 (74.0)	33 (26.0)	0.534
	No	107 (69.9)	46 (30.1)	
DM	Yes	74 (83.1)	15 (16.9)	0.006
	No	127 (66.5)	64 (33.5)	
Smoking	Current Smoker/Tobacco User	80 (68.4)	37 (31.6)	0.347
	Non-Smoker/Ex-Smoker	121 (74.2)	42 (25.8)	
Family History of CAD	Yes	10 (76.9)	3 (23.1)	1.00
	No	190 (71.4)	76 (28.6)	
Type of Statin used	Rosuvastatin	165 (71.7)	65 (28.3)	1.00
	Atorvastatin	36 (72.0)	14 (28.0)	
Atorvastatin dose used	Atorvastatin 20mg	11 (84.6)	2 (15.4)	0.425
	Atorvastatin 40mg	24 (68.6)	11 (31.4)	
	Atorvastatin 80mg	1 (50)	1 (50)	
Rosuvastatin dose used	Rosuvastatin 10mg	3 (75)	1 (25)	0.967
	Rosuvastatin 20mg	140 (71.4)	56 (28.6)	
	Rosuvastatin 40 mg	22 (73.3)	8 (26.7)	

Only 103 (36.8%) achieved more than a 50% decline in LDL-C level after treatment with a statin. Table 4 showed the difference in the proportion of patients achieving a decrease of LDL-C of more than 50% compared to baseline after statin treatment. The difference was also assessed for CVD risk factors, type of statin used, and doses. The 40 mg Rosuvastatin was significantly associated with a decrease of LDL of more than 50% (66.7% vs 33.3%) with a p-value of 0.004. No other CVD risk factors, type of statin used, or other doses of statin used were significantly associated with the decrease in LDL-C.

Table 4.Difference in the proportions achieving required LDL levels of more than 50% and those who didn't for different clinical and management-related characteristics.

		More than 50%	Less than 50%	p-value
HTN	Yes	48 (37.8%)	79 (62.2%)	0.846
	No	55 (35.9%)	98 (64.1%)	
DM	Yes	36 (40.4%)	53 (59.6%)	0.462
	No	67 (35.1%)	124 (64.9%)	
Smoking	Current Smoker/Tobacco User	36 (30.8%)	81 (69.2%)	0.100
	Non-Smoker/Ex-Smoker	67 (41.1%)	96 (58.9%)	
Family History of CAD	Yes	4 (3.8%)	9 (69.2%)	0.774
	No	98 (36.8%)	168 (63.2%)	

Table 4.Difference in the proportions achieving required LDL levels of more than 50% and those who didn't for different clinical and management-related characteristics.				
		More than 50%	Less than 50%	p-value
Type of Statin used	Rosuvastatin	90 (39.1%)	140 (60.9%)	0.113
	Atorvastatin	13 (26.0%)	37 (74.0%)	
Atorvastatin dose used	Atorvastatin 20mg	3 (23.1%)	10 (76.9%)	0.644
	Atorvastatin 40mg	10 (28.6%)	25 (71.4%)	
	Atorvastatin 80mg	0 (0.0%)	2 (100.0%)	
Rosuvastatin dose used	Rosuvastatin 10mg	1 (25.0%)	3 (75.0%)	0.004
	Rosuvastatin 20mg	69 (35.2%)	127 (64.8%)	
	Rosuvastatin 40 mg	20 (66.7%)	10 (33.3%)	

Only 80 (28.6%) achieved the target of both a decrease in LDL-C below 1.4mmol/L as well as more than 50% decrease in LDL-C level from baseline after treatment with a statin. Table 5 demonstrates the proportion of the study population that achieved this target compared to those who did not. When analyzed regarding different CVD risk factors, the type of statin used, and the doses of the statin used, none of the parameters were significantly associated with the achievement of this combined target.

Table 5. Difference in the proportions achieving required LDL levels of less than 1.4mmol/L and more than 50% and those who didn't for different clinical and management-related characteristics.				
		<1.4 and >50%	No	p-value
HTN	Yes	40 (31.5%)	87 (68.5%)	0.393
	No	40 (26.1%)	113 (73.9%)	
DM	Yes	30 (33.7%)	59 (66.3%)	0.247
	No	50 (26.2%)	141 (73.8%)	
Smoking	Current Smoker/Tobacco User	27 (23.1%)	110 (67.5%)	0.112
	Non-Smoker/Ex-Smoker	53 (32.5%)	91 (66.4%)	
Family History of CAD	Yes	2 (15.4%)	11 (84.6%)	0.360
	No	78 (29.3%)	188 (70.7%)	
Type of Statin used	Rosuvastatin	70 (30.4%)	160 (69.6%)	0.191
	Atorvastatin	10 (20.0%)	40 (80.0%)	
Atorvastatin dose used	Atorvastatin 20mg	3 (23.1%)	10 (76.9%)	0.749
	Atorvastatin 40mg	7 (20.0%)	28 (80.0%)	
	Atorvastatin 80mg	0 (0.0%)	2 (100.0%)	
Rosuvastatin dose used	Rosuvastatin 10mg	1 (25.0%)	3 (75.0%)	0.116
	Rosuvastatin 20mg	55 (28.1%)	141 (71.9%)	
	Rosuvastatin 40 mg	14 (46.7%)	16 (53.3%)	

There were 2 (0.7%) participants whose LDL-C levels did not change even after treatment in our study. Table 6 shows the analysis of the CVD risk factors, type of statin used, and its doses associated with the no change in LDL-C level. Use of Rosuvastatin and its all doses used were significantly associated with the change in LDL-C (100%) with a p-value of 0.031.

Table 6. Difference in the proportions achieving no change in LDL levels compared to baseline after the treatment with statin and those who didn't for different clinical and management-related characteristics.

		No change in LDL-C	Change in LDL-C	p-value
HTN	Yes	0 (0.0%)	127 (100.0%)	0.503
	No	2 (1.3%)	151 (98.7%)	
DM	Yes	0 (0.0%)	89 (100.0%)	1.000
	No	2 (1.0%)	189 (99.0%)	
Smoking	Current Smoker/Tobacco User	0 (0.0%)	117 (100.0%)	0.512
	Non-Smoker/Ex-Smoker	2 (1.2%)	161 (98.8%)	
Family History of CAD	Yes	0 (0.0%)	13 (100.0%)	1.000
	No	2 (0.8%)	264 (99.2%)	
Type of Statin used	Rosuvastatin	0 (0.0%)	230 (100.0%)	0.031
	Atorvastatin	2 (4.0%)	48 (96.0%)	
Atorvastatin dose used	Atorvastatin 20mg	0 (0.0%)	13 (100.0%)	0.640
	Atorvastatin 40mg	2 (5.7%)	33 (94.3%)	
	Atorvastatin 80mg	0 (0.0%)	2 (100.0%)	
Rosuvastatin dose used	Rosuvastatin 10mg	0 (0.0%)	4 (100.0%)	NA
	Rosuvastatin 20mg	0 (0.0%)	196 (100.0%)	
	Rosuvastatin 40 mg	0 (0.0%)	30 (100.0%)	

DISCUSSION

In terms of the efficacy of the statin, the present study found that treatment with statins in post-STEMI patients resulted in a significant decrease in total cholesterol and LDL-C levels after 4-12 weeks of follow-up. This is in line with previous studies that have also reported the cholesterol-lowering effects of statins in patients with cardiovascular disease (CVD).[8,9] It is well established that high cholesterol levels, particularly LDL-C, are a major risk factor for the development and progression of CVD.[8] Therefore, the reduction in total cholesterol and LDL-C levels observed in this study is likely to have a positive impact on the long-term outcome of these patients. Furthermore, the study found that 44.6% achieved LDL-C levels below 1.4mmol/l and 71.8% of cases below 1.8mmol/l, with a significantly higher proportion of patients with diabetes mellitus achieving this target (83.1% vs 16.9% after treatment with statins. In addition, the diabetic patients (55.1% and 83.1%) only have the significant achievement of LDL goal of both < 1.4mmol/l and <1.8mmol/l respectively, when compared to those without diabetes (44.9% and 16.9%). One possible explanation might be that the patients with diabetes may have been more closely monitored and had more intensive lipid-lowering therapy. Studies have shown that patients with DM are at a higher risk of cardiovascular disease (CVD) and have a higher baseline LDL-C level.[9,10] Additionally, patients with DM often require more intensive lipid-lowering therapy to achieve guideline-recommended LDL-C targets.[11] Therefore, it is likely that the diabetic patients in this study were receiving more aggressive treatment, which led to a higher proportion of patients achieving the LDL goal of less than 1.4mmol/l. Another possible explanation is that diabetic patients may have had better adherence to the treatment regimen.No other characteristics were significantly associated with the achievement of this LDL-C goal.

This study looked at the effectiveness of statins in reducing cholesterol levels, specifically LDL-C, in post-STEMI patients. The study found that 36.8% of the study population achieved a greater than 50% decline in LDL-C levels. A significantly higher proportion of patients taking Rosuvastatin 40mg had a decrease in LDL-C of more than 50% compared to those who did not (66.7% vs 33.3%). Previous studies have also found that Rosuvastatin is more effective in reducing LDL-C levels compared to other statins. A meta-analysis of randomized controlled trials [12] found that Rosuvastatin was associated with a greater reduction in LDL-C levels compared to atorvastatin, simvastatin, and pravastatin. Another study[13,14] also found that Rosuvastatin 40mg had a greater LDL-C reduction compared to atorvastatin 80mg. However, one of the Indian studies,[15] has found

that both these regimens were found to be equally effective in lowering serum LDL levels.

In this study, the proportion of the study population that had a decrease in LDL-C below 1.4mmol/L as well as more than 50% decrease in LDL-C level from baseline after treatment with a statin was assessed. The results showed that only 28.6% of the patients achieved this target. When analyzed regarding different CVD risk factors, type of statin, and the doses of the statin used, none of the variables were significantly associated with the achievement of this combined target. These findings are in line with previous research for the target LDL-C of less than 1.8mmol/l, EUROASPIRE V (29%)[16] Jankowski et al (28.1%),[17] DYSIS II(18.9%)[4] which showed that statins are effective in reducing LDL-C levels in patients with CAD. Further, the findings for target LDL-C below 1.4 were even low in an Italian study (15%),[18] a French study (18%),[19] in E Harris et al (23.4%).[20] However, the modest level of achievement of LDL-C targets in these studies highlights the need for further research to determine the most effective strategies for achieving optimal LDL-C control in this patient population. This may include the use of combination therapy or the use of more potent statins.

Results of our study also showed that there were 2 (0.7%) participants whose LDL-C levels did not change even after treatment with statins. The difference between those who had no change in LDL-C and those who had changes in LDL-C were assessed for CVD risk factors, type of statin used, and its doses. The use of Rosuvastatin was significantly associated with the change in LDL-C. Further research is needed to understand the reasons for this association and to determine if there are any clinical implications.

As per the latest European guidelines,[20] high-intensity Lipid-lowering treatment should be started as early as possible, as this increases patient adherence after discharge. In our study, Rosuvastatin was the preferred choice of statin among STEMI patients, with 82.1% of patients, and the 20mg dose is mostly prescribed (70%). The remaining 17.9% of patients were prescribed Atorvastatin. Rosuvastatin 40mg (10.7%) and Atorvastatin 80mg (0.7%) were the least used doses. In contrast to our study, several other studies have different scenarios. In Hongkong study[21] and the German study, [22] simvastatin was widely used (65.78%, 54.9%) followed by relatively little use of rosuvastatin (7.04%, 6.7%) and atorvastatin (4.44%, 31.6%). Further in POLASPIRE Survey [23] atorvastatin was more prevalent (97.01% and 77.1%) respectively. It should be noted that while any statin is most commonly prescribed, it may not be appropriate or the best option for all patients, as patient/physician's preferences, comorbidities, and other factors may influence the choice of medication. Studies should be done in different populations and practice settings to generalize it. The higher dose of Atorvastatin is less used which could be due to the physician's choice and the practice setting.

Overall, these findings provide insight into the effectiveness of statin use in achieving LDL-C targets in patients with ST-elevation MI and suggest the need for further research to optimize LDL-C control in this patient population. It is important to consider the potential impact of CVD risk factors and the type and dose of statins on LDL-C levels in the management of patients with ST-elevation MI.

There are a few limitations in our study, The first limitation of the study is that there were no stratified data of outcome based on the severity of the disease at presentation and comorbidities at presentation. It is worth noting that this study only looked at the changes in lipid parameters and did not investigate the effect of statin treatment on other outcomes such as mortality or recurrent myocardial infarction. The study enrolled patients from a single center; hence, the applicability of results to general clinical practice may be limited. Lastly, since we collected data from a single follow-up of 4-12 weeks, the study was not designed to gather sufficient data on morbidity and mortality, and could not infer any conclusion on the association between specific post-STEMI LDL-C levels and morbidity and mortality. On this note, we suggest conducting an extensive and multicenter study for the evaluation of morbidity and mortality.

CONCLUSIONS

The study found that most of the post-STEMI patients treated with high doses of statins achieved the target LDL-C levels below 1.8mmol/l (73.8%) with Rosuvastatin 20mg dose being the most commonly prescribed. Furthermore, 44.6% of patients achieved LDL-C levels below 1.4mmol/l, with a higher proportion of diabetic patients achieving this target.

CONFLICT OF INTEREST

None to declare.

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